

REMARKS

Claims 15-29 are currently pending. Of these, claims 19 and 26-29 have been set aside in response to a restriction requirement issued on March 6, 2008. Thus, claims 15, 16, and 17 are the pending independent claims. In the Office Action, the Examiner rejected Claims 15 – 18, 20 – 22, and 24 – 26 as allegedly obvious under 35 U.S.C. § 103(a) based on U.S. Patent No. 4,935,429 to Dackis et al. (“Dackis”) in combination with U.S. Patent No. 5,480,885 to Rucman et al. (“Rucman”) and in further view of Smelson (Canadian Journal of Psychiatry, 2002) (“Smelson”). Claim 23 was rejected as allegedly obvious under 35 U.S.C. § 103(a) based on Dackis combined with both Rucman and Glavan (Molecular Pharmacology, 2002) (“Glavan”).

Each of the foregoing rejections is respectfully traversed and favorable reconsideration is requested in view of the following remarks.

I. The § 103(a) Rejections of Claims 15-18, 20-22, and 24-26

All of the pending independent claims (i.e., claims 15 - 17) are directed to a method for the treatment of psychostimulant addiction and require, *inter alia*, administering to the patient a pharmacologically acceptable form of 9,10-didehydro-N-methyl-N-(2-propynyl)-6-methyl-8 β -aminomethylergoline as a partial dopamine agonist.

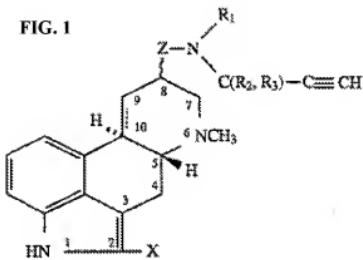
The Examiner has cited various combinations of three different references in an effort to support his rejection of claims 15 – 18, 20 – 22, and 24 – 26. The first cited reference, Dackis, describes the use of a dopamine **agonist** bromocriptine to treat psychostimulant addiction. There is no mention in Dackis of the use of 9,10- didehydro-N-methyl-N-(2-propynyl)-6-methyl-8 β -aminomethylergoline for any purpose whatsoever, much less to treat any symptoms associated with any type of narcotic addition. Rucman teaches the use of ergolinyl derivatives of 2-propynylamine of the genus shown in Figure 1 (below) for treating a mental illness. Rucman says “the novel ergoline derivatives of the present invention possess an extraordinary potent antipsychotic and *potentially* anxiolytic and antidepressant action.” Rucman, Column 3, lines 46-47 (emphasis added). Rucman makes no mention of use of any so-called ergoline derivatives for the treatment of psychostimulant addiction withdrawal symptoms. Again, Rucman observes that “the novel ergoline derivatives of the present invention exhibit strong **antagonistic** action on D₂ and 5-HT₂ receptors and weak action on the

level of α_1 receptors" Rucman, Column 3, lines 19-21 (emphasis added). Rucman does mention 9,10-didehydro-N-methyl-N-(2-propynyl)-6-methyl-8 β -aminomethylergoline as one example of an agent that is said to be useful in the treatment of a mental illness. On the other hand, Smelson describes the use of Risperidone for treating cocaine dependence. And Risperidone has also been used to treat schizophrenia. But this can hardly be taken as a general or broad teaching that all pharmaceuticals said to be useful for treating mental illnesses would also be expected to be useful to treat symptoms of withdrawal of narcotic addition.

In the Office Action, the Examiner asserts that a person having ordinary skill in the art would be motivated to combine Dackis and Rucman as follows: "The motivation is that one would expect with a reasonable degree of success that similar results will be obtained by substituting one ergoline derivative for another, *in the absence of unexpected results*, in particular when both derivatives are *agonists* at the dopamine receptor." The Examiner has made no specific assertion with regard to combining Smelson with Dackis and Rucman, so, to the extent that the Examiner relies on Smelson, Applicants respectfully assert that the Examiner has failed to make even a *prima facie* case of obviousness.

Regardless of the inclusion of Smelson, a combination of the teachings of Dackis with those of Rucman towards the present invention is improper for at least the following reasons. First, Applicants' specification contains experiments that demonstrate "truly unexpected and surprising" results which exactly defeat the purported logic of the Examiner's argument. Examples in Applicants' specification compare the relevant psychotropic effect of bromocriptine with that of 9,10-didehydro-N-methyl-N-(2-propynyl)-6-methyl-8 β -aminomethylergoline relative to cocaine-craving symptoms. U.S. Pat. App. Pub. No. 2006/0014775, [0020] - [0021]. Although the two drugs may be structurally very similar, the psychotropic effects vis-à-vis cocaine dependency factors were found to be notably different. These experiments showed that 9,10-didehydro-N-methyl-N-(2-propynyl)-6-methyl-8 β -

FIG. 1



aminomethylergoline exhibited no “additive potential as exhibited by cocaine but it prevents the effects of cocaine.” U.S. Pat. App. Pub. No. 2006/0014775, [0030]. In contrast, Bromocriptine was shown to “not prevent the relapse to cocaine dependence, and at certain doses it even [has] caused a relapse itself or proved to be addictive.” U.S. Pat. App. Pub. No. 2006/0014775, [0047] (citing Wise et al., 1990). These are precisely the kind of “unexpected” and “surprising” results that defeat any contention that it would have been obvious to expect dependency-related effects from administration of 9,10-didehydro-N-methyl-N-(2-propynyl)-6-methyl-8 β -aminomethylergoline would be similar to those of Bromocriptine.

Second, with regard to the motivation for combining Dackis and Rucman, Dackis describes the dopamine receptor *agonist* bromocriptine and related derivatives to treat psychostimulant addiction. See Dackis, Column 2, lines 49-50. In contrast, Rucman describes various chemical species with a focus on their dopamine (D₂) receptor *antagonist* properties for treating psychosis. See Rucman, Column 4, lines 19 - 21. These references therefore deal with essentially opposite features of the respective drugs. Thus, at the time of the invention, a person of ordinary skill would not be motivated to apply teachings of Dackis to those of Rucman to achieve anything cohesive relative to use of their respective pharmaceuticals, much less what is claimed in the present application.

Finally, as the Examiner is surely aware, the efficacy of psychotropic drugs for various applications is generally not predictable. The types of receptors in the brain for these effects are not even thought to be fully identified yet. Unlike, for example, mechanical arts, a first chemical species in a complex biological environment may behave and/or cause effects that are totally different than a very similar second chemical species. The present disclosure is an example of such phenomena.

In light of the arguments set forth above, Applicants respectfully submit that the combination of Dackis and Rucman (and Smelson, if applicable) does not lawfully render claims 15 - 17 obvious under § 103(a). Accordingly, claims 15 - 17 patentably define over Dackis in view of Rucman. Reconsideration and allowance of claims 15 - 17 are respectfully requested.

Dependent claims 18, 20 - 22, and 24 – 26 depend from independent claims 15 - 17, and contain additional important aspects of the invention. Therefore, dependent claims 18, 20 - 22,

Application No. 10/539,501
July 29, 2008

and 24 – 26 patentably define over Dackis in view of Rucman. Reconsideration and allowance of dependent claims 18, 20 - 22, and 24 – 26 are respectfully requested.

II. The § 103(a) Rejection of Claim 23

The arguments from Section I (above) are incorporated herein by reference. Dependent claim 23 depends from independent claim 15, and contains additional important aspects of the invention. Glavan addresses the use of the bimaleinate salt form of 9,10-didehydro-N-methyl-N-(2-propynyl)-6-methyl-8 β -aminomethylergoline as an *experimental anti-psychotic* medicament but does not compensate for (1) the fact Applicants' disclosure covers experimental results using 9,10-didehydro-N-methyl-N-(2-propynyl)-6-methyl-8 β -aminomethylergoline for psychostimulant addiction treatment that were totally unexpected and/or (2) the deficiencies of the improper combination of Dackis and Rucman described above. Therefore, dependent claim 23 patentably defines over Dackis in view of Rucman and Glavan. Reconsideration and allowance of dependent claim 23 are respectfully requested.

In light of the foregoing, Applicants respectfully request the Examiner reconsider the application, withdraw the rejections, and issue a notice of allowance at the earliest possible convenience.

In the event this response is not timely filed, Applicants hereby petition for the appropriate extension of time and request that the fee for the extension along with any other fees which may be due with respect to this paper be charged to our Deposit Account No. 12-2355.

Respectfully submitted,
LUEDEKA, NEELY & GRAHAM, P.C.
By: /Mark S. Graham/
Mark S. Graham
Registration No. 32,355

Date: July 29, 2008
P.O. Box 1871
Knoxville, Tennessee 37901
(865) 546-4305